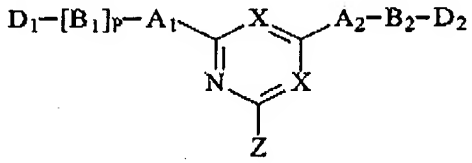
In the Claims

This listing of claims will replace all prior versions and listings of claims in this application.

1 (original). An affinity ligand-matrix conjugate comprising the matrix and, conjugated thereto by the group Z, a ligand having the general formula (I):



wherein one X is N and the other X is N, CCl or CCN;

A_1 and A_2 are each independently O, S or N-R_1 and R_1 is H, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, benzyl or β-phenylethyl;

B_1 and B_2 are each independently an optionally substituted hydrocarbon linkage containing from 1 to 10 carbon atoms;

D_1 is H or a primary amino, secondary amino, tertiary amino, quaternary ammonium, imidazole, guanidine or amidino group; and

D_2 is a secondary amino, tertiary amino, quaternary ammonium, imidazole, guanidine or amidino group; or

B_2-D_2 is -CHCOOH-$(CH_2)_{3-4}$-NH_2; and

p is 0 or 1;

with the proviso that, when each X is N, A_1 is NR_1, A_2 is NH, B_2 is phenyl, D_1 is H, D_2 is amidino and p is zero, then R_1 is not methyl, β-phenylethyl or β-hydroxyethyl.

2 (previously presented). The conjugate according to claim 1, wherein A_1 and A_2 are each independently N-R_1 wherein R_1 is H, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, benzyl or β-phenylethyl.

3 (previously presented). The conjugate according to claim 2, wherein A_1 and A_2 are each NH.

4 (previously presented). The conjugate according to claim 1, wherein B_1 and B_2 are each independently -CHCOOH-$(CH_2)_{1-4}$- or a divalent ethyl, propyl, 2-hydroxypropyl, butyl, pentyl, hexyl, phenyl, naphthyl or cyclohexyl group.

5 (previously presented). The conjugate according to claim 4, wherein B_1 and B_2 are each independently -CHCOOH-$(CH_2)_{3-4}$- or a divalent butyl, pentyl or phenyl group.

6 (previously presented). The conjugate according to claim 4, wherein B_1 and B_2 are each independently -CHCOOH-$(CH_2)_{3-4}$- and p is 1.

7 (previously presented). The conjugate according to claim 1, wherein D_1 is H, amino, imidazolyl, guanidine, aminidino, trimethylammonium, triethylammonium, dimethylamino, diethylamino, methylamino or ethylamino.

8 (previously presented). The conjugate according to [any preceding] claim 1, wherein D_2 is imidazolyl, guanidine, aminidino, trimethylammonium, triethylammonium, dimethylamino, diethylamino, methylamino or ethylamino.

9 (previously presented). The conjugate according to claim 1, wherein p is 1.

10 (previously presented). The conjugate according to claim 1, wherein each X is N.

11 (previously presented). The conjugate according to claim 1, wherein Z is

$$-T-[L-V]_m- \qquad (II)$$

wherein T is O, S or NR_2 and R_2 is H or C_{1-6} alkyl;

V is O, S, -COO-, CONH, NHCO, $-PO_3H-$, NH-arylene-$SO_2-CH_2-CH_2-$ or N-R_3 and R_3 is H or C_{1-6} alkyl;

L is an optionally substituted hydrocarbon linkage containing from 2 to 20 carbon atoms; and

m is 0 or 1.

12 (previously presented). The conjugate according to claim 11, wherein R_2 and R_3 are each H.

13 (previously presented). The conjugate according to claim 11, wherein T is O or NH.

14 (previously presented). The conjugate according to claim 13, wherein T is NH.

15 (previously presented). The conjugate according to claim 1 , wherein m is 1 and L is a divalent butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl or dodecyl group.

16 (previously presented). The conjugate according to claim 11, wherein m is 1 and V is O, -CONH-, -NHCO- or N-R_3.

17 (previously presented). The conjugate according to claim 16, wherein V is O or NH.

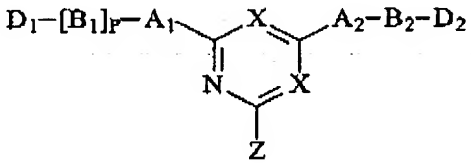
18 (previously presented). The conjugate according to claim 17, wherein V is NH.

19 (previously presented). The conjugate according to claim 17, wherein Z-M (M being the matrix) is -NH-$(CH_2)_{4-10}$-NH-M.

20 (previously presented). The conjugate according to claim 19, selected from any of formulae XXX to XXXX.

21 (previously presented). The conjugate according to claim 1, wherein the matrix is optionally tresyl-activated, sulphonyl chloride-activated, tosyl-activated, vinyl sulphone-activated or epoxy-activated.

22 (previously presented). An affinity ligand of general formula (I):



(I)

wherein one X is N and the other X is N, CCl or CCN;

A_1 and A_2 are each independently O, S or N-R_1 and R_1 is H, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, benzyl or β-phenylethyl;

B_1 and B_2 are each independently an optionally substituted hydrocarbon linkage containing from 1 to 10 carbon atoms;

D_1 is H or a primary amino, secondary amino, tertiary amino, quaternary ammonium, imidazole, guanidine or amidino group; and

D_2 is a secondary amino, tertiary amino, quaternary ammonium, imidazole, guanidine or amidino group; or

B_2-D_2 is -CHCOOH-$(CH_2)_{3-4}$-NH_2; and

p is 0 or 1; and

wherein Z is a functional group capable of reaction with a solid matrix; and with the proviso that, when each X is N, A_1 is NR_1, A_2 is NH, B_2 is phenyl, D_1 is H, D_2 is amidino and p is zero, then R_1 is not methyl, β-phenylethyl or β-hydroxyethyl.

23 (previously presented). The ligand according to claim 22, wherein the matrix is optionally tresyl-activated, sulphonyl chloride-activated, tosyl-activated, vinyl sulphone-activated or epoxy-activated.

24 (previously presented). The ligand according to claim 22, wherein Z is F, Cl, Br or I.

25 (previously presented). The ligand according to claim 22, wherein Z is -NH-$(CH_2)_{2-20}$-NH_2.

26 (previously presented). The ligand according to claim 22, wherein Z is -NH-$(CH_2)_{2-20}$-$(CO)_{0-1}$-OH.

27 (previously presented). The ligand according to claim 22, wherein Z is

-T-[L-V]$_m$-R_{10}-CR_{11}=CH_2

wherein T is O, S or NR_2 and R_2 is H or C_{1-6} alkyl;

V is O, S, -COO-, CONH, NHCO, -PO_3H-, NH-arylene-SO_2-CH_2-CH_2- or N-R_3 and R_3 is H or C_{1-6} alkyl;

L is an optionally substituted hydrocarbon linkage containing from 2 to 20 carbon atoms;

m is 0 or 1;

R_{10} is CO, CH_2, NH-CH_2- or -S-CH_2-; and

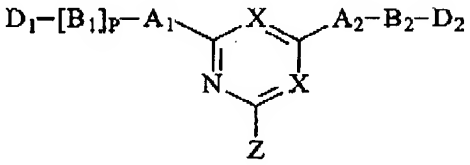
R_{11} is H or C_{1-6} alkyl.

28 (previously presented). The ligand according to claim 24, wherein Z is Cl, and each X is N.

29 (previously presented). The ligand according to claim 28, wherein each X is N.

30 (previously presented). The ligand according to claim 22, selected from any of formulae XVI to XXVI.

31 (currently amended). A method for the removal, separation, isolation, purification, characterization, identification or quantification of an endotoxin; wherein said method utilizes an affinity ligand or conjugate having the general formula (I):



(I)

wherein one X is N and the other X is N, CCl or CCN;

Z is a functional group capable of reaction with a solid matrix;

A_1 and A_2 are each independently O, S or N-R_1 and R_1 is H, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, benzyl or β-phenylethyl;

B_1 and B_2 are each independently an optionally substituted hydrocarbon linkage containing from 1 to 10 carbon atoms;

D_1 is H or a primary amino, secondary amino, tertiary amino, quaternary ammonium, imidazole, guanidine or amidino group; and

D_2 is a secondary amino, tertiary amino, quaternary ammonium, imidazole, guanidine or amidino group; or

B_2-D_2 is -CHCOOH-$(CH_2)_{3-4}$-NH_2; and

p is 0 or 1.

32 (previously presented). The method according to claim 31, for the removal of an endotoxin from water or an aqueous solution, body fluid, blood, plasma, solution of pharmaceutical products, protein or other compound of biological origin.

33 (previously presented). The method according to claim 32, which comprises using the conjugate for the extracorporeal removal of endotoxin from whole blood or plasma, prior to re-infusion into the door or another recipient.

34 (previously presented). The method according to claim 31, wherein the endotoxin originates from a Gram-negative bacterium.

35 (previously presented). The method according to claim 31, in an endotoxin-containing solution or liquid is applied to the conjugate at a pH of 1.0 to 13.0.